IN THE SPECIFICATION:

Please replace the paragraphs at page 2, lines 13-33, with the following paragraphs:

In one aspect, the invention provides an isolated NOVX nucleic acid molecule encoding a NOVX polypeptide that includes a nucleic acid sequence that has identity to the nucleic acids disclosed in SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101. In some embodiments, the NOVX nucleic acid molecule will hybridize under stringent conditions to a nucleic acid sequence complementary to a nucleic acid molecule that includes a protein-coding sequence of a NOVX nucleic acid sequence. The invention also includes an isolated nucleic acid that encodes a NOVX polypeptide, or a fragment, homolog, analog or derivative thereof. For example, the nucleic acid can encode a polypeptide at least 80% identical to a polypeptide comprising the amino acid sequences of SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102. The nucleic acid can be, for example, a genomic DNA fragment or a cDNA molecule that includes the nucleic acid sequence of any of SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101.

Also included in the invention is an oligonucleotide, *e.g.*, an oligonucleotide which includes at least 6 contiguous nucleotides of a NOVX nucleic acid (*e.g.*, SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101) or a complement of said oligonucleotide.

Also included in the invention are substantially purified NOVX polypeptides (SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102). In certain embodiments, the NOVX polypeptides include an amino acid sequence that is substantially identical to the amino acid sequence of a human NOVX polypeptide.

Please replace the paragraphs at page 131, line 31 through page 132, line 33, with the following paragraphs:

A nucleic acid molecule of the invention, *e.g.*, a nucleic acid molecule having the nucleotide sequence SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101, or a complement of this aforementioned nucleotide sequence, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or a portion of the nucleic

acid sequence of SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101 as a hybridization probe, NOVX molecules can be isolated using standard hybridization and cloning techniques (*e.g.*, as described in Sambrook, *et al.*, (eds.), MOLECULAR CLONING: A LABORATORY MANUAL 2nd Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989; and Ausubel, *et al.*, (eds.), CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, New York, NY, 1993.)

A nucleic acid of the invention can be amplified using cDNA, mRNA or alternatively, genomic DNA, as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. The nucleic acid so amplified can be cloned into an appropriate vector and characterized by DNA sequence analysis. Furthermore, oligonucleotides corresponding to NOVX nucleotide sequences can be prepared by standard synthetic techniques, *e.g.*, using an automated DNA synthesizer.

As used herein, the term "oligonucleotide" refers to a series of linked nucleotide residues, which oligonucleotide has a sufficient number of nucleotide bases to be used in a PCR reaction. A short oligonucleotide sequence may be based on, or designed from, a genomic or cDNA sequence and is used to amplify, confirm, or reveal the presence of an identical, similar or complementary DNA or RNA in a particular cell or tissue. Oligonucleotides comprise portions of a nucleic acid sequence having about 10 nt, 50 nt, or 100 nt in length, preferably about 15 nt to 30 nt in length. In one embodiment of the invention, an oligonucleotide comprising a nucleic acid molecule less than 100 nt in length would further comprise at least 6 contiguous nucleotides SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101, or a complement thereof. Oligonucleotides may be chemically synthesized and may also be used as probes.

In another embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule that is a complement of the nucleotide sequence shown in SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101, or a portion of this nucleotide sequence (*e.g.*, a fragment that can be used as a probe or primer or a fragment encoding a biologically-active portion of an NOVX polypeptide). A nucleic acid molecule that is complementary to the nucleotide sequence shown SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101 is one that is sufficiently complementary to the nucleotide sequence shown SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101 that it can hydrogen bond with little or no mismatches to the nucleotide sequence shown SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65,~~

~~71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101, thereby forming a stable duplex.

Please replace the paragraph at page 134, lines 21-31, with the following paragraph:

The nucleotide sequences determined from the cloning of the human NOVX genes allows for the generation of probes and primers designed for use in identifying and/or cloning NOVX homologues in other cell types, *e.g.* from other tissues, as well as NOVX homologues from other vertebrates. The probe/primer typically comprises substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, 25, 50, 100, 150, 200, 250, 300, 350 or 400 consecutive sense strand nucleotide sequence SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101; or an anti-sense strand nucleotide sequence of SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101; or of a naturally occurring mutant of SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101.

Please replace the paragraph at page 135, lines 5-13, with the following paragraph:

"A polypeptide having a biologically-active portion of an NOVX polypeptide" refers to polypeptides exhibiting activity similar, but not necessarily identical to, an activity of a polypeptide of the invention, including mature forms, as measured in a particular biological assay, with or without dose dependency. A nucleic acid fragment encoding a "biologically-active portion of NOVX" can be prepared by isolating a portion SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101, that encodes a polypeptide having an NOVX biological activity (the biological activities of the NOVX proteins are described below), expressing the encoded portion of NOVX protein (*e.g.*, by recombinant expression *in vitro*) and assessing the activity of the encoded portion of NOVX.

Please replace the paragraphs at page 135, line 15, through page 136, line 17, with the following paragraphs:

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequences shown in SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101 due to degeneracy of the genetic code and thus encode the same NOVX proteins as that encoded

by the nucleotide sequences shown in SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101. In another embodiment, an isolated nucleic acid molecule of the invention has a nucleotide sequence encoding a protein having an amino acid sequence shown in SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102.

In addition to the human NOVX nucleotide sequences shown in SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101, it will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences of the NOVX polypeptides may exist within a population (*e.g.*, the human population). Such genetic polymorphism in the NOVX genes may exist among individuals within a population due to natural allelic variation. As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules comprising an open reading frame (ORF) encoding an NOVX protein, preferably a vertebrate NOVX protein. Such natural allelic variations can typically result in 1-5% variance in the nucleotide sequence of the NOVX genes. Any and all such nucleotide variations and resulting amino acid polymorphisms in the NOVX polypeptides, which are the result of natural allelic variation and that do not alter the functional activity of the NOVX polypeptides, are intended to be within the scope of the invention.

Moreover, nucleic acid molecules encoding NOVX proteins from other species, and thus that have a nucleotide sequence that differs from the human SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101 are intended to be within the scope of the invention. Nucleic acid molecules corresponding to natural allelic variants and homologues of the NOVX cDNAs of the invention can be isolated based on their homology to the human NOVX nucleic acids disclosed herein using the human cDNAs, or a portion thereof, as a hybridization probe according to standard hybridization techniques under stringent hybridization conditions.

Accordingly, in another embodiment, an isolated nucleic acid molecule of the invention is at least 6 nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101. In another embodiment, the nucleic acid is at least 10, 25, 50, 100, 250, 500, 750, 1000, 1500, or 2000 or more nucleotides in length. In yet another embodiment, an isolated nucleic acid molecule of the invention hybridizes to the coding region. As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 60% homologous to each other typically remain hybridized to each other.

Please replace the paragraphs at page 137, line 3, through page 139, line 25, with the following paragraphs:

Stringent conditions are known to those skilled in the art and can be found in Ausubel, *et al.*, (eds.), CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. Preferably, the conditions are such that sequences at least about 65%, 70%, 75%, 85%, 90%, 95%, 98%, or 99% homologous to each other typically remain hybridized to each other. A non-limiting example of stringent hybridization conditions are hybridization in a high salt buffer comprising 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 mg/ml denatured salmon sperm DNA at 65°C, followed by one or more washes in 0.2X SSC, 0.01% BSA at 50°C. An isolated nucleic acid molecule of the invention that hybridizes under stringent conditions to the sequences SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101, corresponds to a naturally-occurring nucleic acid molecule. As used herein, a "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in nature (*e.g.*, encodes a natural protein).

In a second embodiment, a nucleic acid sequence that is hybridizable to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101, or fragments, analogs or derivatives thereof, under conditions of moderate stringency is provided. A non-limiting example of moderate stringency hybridization conditions are hybridization in 6X SSC, 5X Denhardt's solution, 0.5% SDS and 100 mg/ml denatured salmon sperm DNA at 55°C, followed by one or more washes in 1X SSC, 0.1% SDS at 37°C. Other conditions of moderate stringency that may be used are well-known within the art. *See, e.g.*, Ausubel, et *al.* (eds.), 1993, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, NY, and Kriegler, 1990; GENE TRANSFER AND EXPRESSION, A LABORATORY MANUAL, Stockton Press, NY.

In a third embodiment, a nucleic acid that is hybridizable to the nucleic acid molecule comprising the nucleotide sequences SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101, or fragments, analogs or derivatives thereof, under conditions of low stringency, is provided. A non-limiting example of low stringency hybridization conditions are hybridization in 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 mg/ml denatured salmon sperm DNA, 10% (wt/vol) dextran sulfate at 40°C, followed by one or more washes in 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS at 50°C. Other conditions of low stringency that may be used are well known in the art (*e.g.*, as employed for cross-species hybridizations).

See, e.g., Ausubel, *et al.* (eds.), 1993, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, NY, and Kriegler, 1990, GENE TRANSFER AND EXPRESSION, A LABORATORY MANUAL, Stockton Press, NY; Shilo and Weinberg, 1981. *Proc Natl Acad Sci USA* **78**: 6789-6792.

Conservative Mutations

In addition to naturally-occurring allelic variants of NOVX sequences that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequences SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101, thereby leading to changes in the amino acid sequences of the encoded NOVX proteins, without altering the functional ability of said NOVX proteins. For example, nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues can be made in the sequence SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequences of the NOVX proteins without altering their biological activity, whereas an "essential" amino acid residue is required for such biological activity. For example, amino acid residues that are conserved among the NOVX proteins of the invention are predicted to be particularly non-amenable to alteration. Amino acids for which conservative substitutions can be made are well-known within the art.

Another aspect of the invention pertains to nucleic acid molecules encoding NOVX proteins that contain changes in amino acid residues that are not essential for activity. Such NOVX proteins differ in amino acid sequence from SEQ ID NOS:2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102 yet retain biological activity. In one embodiment, the isolated nucleic acid molecule comprises a nucleotide sequence encoding a protein, wherein the protein comprises an amino acid sequence at least about 45% homologous to the amino acid sequences SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102. Preferably, the protein encoded by the nucleic acid molecule is at least about 60% homologous to SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102; more preferably at least about 70% homologous SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102; still more preferably at least about 80% homologous to SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102; even more preferably at least about 90% homologous to SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36,~~

~~42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102; and most preferably at least about 95% homologous to SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102.

An isolated nucleic acid molecule encoding an NOVX protein homologous to the protein of SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102 can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101, such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein.

Mutations can be introduced into SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101 by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted, non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined within the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted non-essential amino acid residue in the NOVX protein is replaced with another amino acid residue from the same side chain family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of an NOVX coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for NOVX biological activity to identify mutants that retain activity. Following mutagenesis of SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101, the encoded protein can be expressed by any recombinant technology known in the art and the activity of the protein can be determined.

Please replace the paragraph at page 140, lines 7-20, with the following paragraph:

Another aspect of the invention pertains to isolated antisense nucleic acid molecules that are hybridizable to or complementary to the nucleic acid molecule comprising the nucleotide sequence of

SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101, or fragments, analogs or derivatives thereof. An "antisense" nucleic acid comprises a nucleotide sequence that is complementary to a "sense" nucleic acid encoding a protein (*e.g.*, complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence). In specific aspects, antisense nucleic acid molecules are provided that comprise a sequence complementary to at least about 10, 25, 50, 100, 250 or 500 nucleotides or an entire NOVX coding strand, or to only a portion thereof. Nucleic acid molecules encoding fragments, homologs, derivatives and analogs of an NOVX protein of SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102, or antisense nucleic acids complementary to an NOVX nucleic acid sequence of SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101, are additionally provided.

Please replace the paragraph at page 142, lines 20-33, with the following paragraph:

In one embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity that are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (*e.g.*, hammerhead ribozymes as described in Haselhoff and Gerlach 1988. *Nature* 334: 585-591) can be used to catalytically cleave NOVX mRNA transcripts to thereby inhibit translation of NOVX mRNA. A ribozyme having specificity for an NOVX-encoding nucleic acid can be designed based upon the nucleotide sequence of an NOVX cDNA disclosed herein (*i.e.*, SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101). For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in an NOVX-encoding mRNA. *See*, *e.g.*, U.S. Patent 4,987,071 to Cech, *et al.* and U.S. Patent 5,116,742 to Cech, *et al.* NOVX mRNA can also be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. *See*, *e.g.*, Bartel *et al.*, (1993) *Science* 261:1411-1418.

Please replace the paragraph at page 144, lines 17-24, with the following paragraph:

A polypeptide according to the invention includes a polypeptide including the amino acid sequence of NOVX polypeptides whose sequences are provided in SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102. The invention also includes a mutant or variant

protein any of whose residues may be changed from the corresponding residues shown in SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102 while still encoding a protein that maintains its NOVX activities and physiological functions, or a functional fragment thereof.

Please replace the paragraphs at page 145, line 29, through page 146, line 17, with the following paragraphs:

Biologically-active portions of NOVX proteins include peptides comprising amino acid sequences sufficiently homologous to or derived from the amino acid sequences of the NOVX proteins (*e.g.*, the amino acid sequence shown in SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102) that include fewer amino acids than the full-length NOVX proteins, and exhibit at least one activity of an NOVX protein. Typically, biologically-active portions comprise a domain or motif with at least one activity of the NOVX protein. A biologically-active portion of an NOVX protein can be a polypeptide which is, for example, 10, 25, 50, 100 or more amino acid residues in length.

Moreover, other biologically-active portions, in which other regions of the protein are deleted, can be prepared by recombinant techniques and evaluated for one or more of the functional activities of a native NOVX protein.

In an embodiment, the NOVX protein has an amino acid sequence shown SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102. In other embodiments, the NOVX protein is substantially homologous to SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102, and retains the functional activity of the protein of SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102, yet differs in amino acid sequence due to natural allelic variation or mutagenesis, as described in detail, below. Accordingly, in another embodiment, the NOVX protein is a protein that comprises an amino acid sequence at least about 45% homologous to the amino acid sequence SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102, and retains the functional activity of the NOVX proteins of SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102.

Please replace the paragraph at page 146, line 28, through page 147, line 2, with the following paragraph:

The nucleic acid sequence homology may be determined as the degree of identity between two sequences. The homology may be determined using computer programs known in the art, such as GAP software provided in the GCG program package. *See,* Needleman and Wunsch, 1970. *J Mol Biol* 48: 443-453. Using GCG GAP software with the following settings for nucleic acid sequence comparison: GAP creation penalty of 5.0 and GAP extension penalty of 0.3, the coding region of the analogous nucleic acid sequences referred to above exhibits a degree of identity preferably of at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99%, with the CDS (encoding) part of the DNA sequence shown in SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101.

Please replace the paragraph at page 147, lines 18-34, with the following paragraph:

The invention also provides NOVX chimeric or fusion proteins. As used herein, an NOVX "chimeric protein" or "fusion protein" comprises an NOVX polypeptide operatively-linked to a non-NOVX polypeptide. An "NOVX polypeptide" refers to a polypeptide having an amino acid sequence corresponding to an NOVX protein SEQ ID NOS:~~1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101~~ 2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102), whereas a "non-NOVX polypeptide" refers to a polypeptide having an amino acid sequence corresponding to a protein that is not substantially homologous to the NOVX protein, *e.g.*, a protein that is different from the NOVX protein and that is derived from the same or a different organism. Within an NOVX fusion protein the NOVX polypeptide can correspond to all or a portion of an NOVX protein. In one embodiment, an NOVX fusion protein comprises at least one biologically-active portion of an NOVX protein. In another embodiment, an NOVX fusion protein comprises at least two biologically-active portions of an NOVX protein. In yet another embodiment, an NOVX fusion protein comprises at least three biologically-active portions of an NOVX protein. Within the fusion protein, the term "operatively-linked" is intended to indicate that the NOVX polypeptide and the non-NOVX polypeptide are fused in-frame with one another. The non-NOVX polypeptide can be fused to the N-terminus or C-terminus of the NOVX polypeptide.

Please replace the paragraphs at page 167, lines 3-33, with the following paragraphs:

A transgenic animal of the invention can be created by introducing NOVX-encoding nucleic acid into the male pronuclei of a fertilized oocyte (*e.g.*, by microinjection, retroviral infection) and allowing the oocyte to develop in a pseudopregnant female foster animal. The human NOVX cDNA sequences SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12,

18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101 can be introduced as a transgene into the genome of a non-human animal. Alternatively, a non-human homologue of the human NOVX gene, such as a mouse NOVX gene, can be isolated based on hybridization to the human NOVX cDNA (described further *supra*) and used as a transgene. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably-linked to the NOVX transgene to direct expression of NOVX protein to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866; 4,870,009; and 4,873,191; and Hogan, 1986. In: MANIPULATING THE MOUSE EMBRYO, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of the NOVX transgene in its genome and/or expression of NOVX mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene-encoding NOVX protein can further be bred to other transgenic animals carrying other transgenes.

To create a homologous recombinant animal, a vector is prepared which contains at least a portion of an NOVX gene into which a deletion, addition or substitution has been introduced to thereby alter, *e.g.*, functionally disrupt, the NOVX gene. The NOVX gene can be a human gene (*e.g.*, the cDNA of SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101), but more preferably, is a non-human homologue of a human NOVX gene. For example, a mouse homologue of human NOVX gene of SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101 can be used to construct a homologous recombination vector suitable for altering an endogenous NOVX gene in the mouse genome. In one embodiment, the vector is designed such that, upon homologous recombination, the endogenous NOVX gene is functionally disrupted (*i.e.*, no longer encodes a functional protein; also referred to as a "knock out" vector).

Please replace the paragraph at page 178, lines 27-33, with the following paragraph:

Once the sequence (or a portion of the sequence) of a gene has been isolated, this sequence can be used to map the location of the gene on a chromosome. This process is called chromosome mapping. Accordingly, portions or fragments of the NOVX sequences, SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101, or fragments or derivatives thereof, can be used to map

the location of the NOVX genes, respectively, on a chromosome. The mapping of the NOVX sequences to chromosomes is an important first step in correlating these sequences with genes associated with disease.

Please replace the paragraph at page 181, lines 10-17, with the following paragraph:

Each of the sequences described herein can, to some degree, be used as a standard against which DNA from an individual can be compared for identification purposes. Because greater numbers of polymorphisms occur in the noncoding regions, fewer sequences are necessary to differentiate individuals. The noncoding sequences can comfortably provide positive individual identification with a panel of perhaps 10 to 1,000 primers that each yield a noncoding amplified sequence of 100 bases. If predicted coding sequences, such as those in SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101 are used, a more appropriate number of primers for positive individual identification would be 500-2,000.

Please replace the paragraph at page 182, lines 14-25, with the following paragraph:

An exemplary method for detecting the presence or absence of NOVX in a biological sample involves obtaining a biological sample from a test subject and contacting the biological sample with a compound or an agent capable of detecting NOVX protein or nucleic acid (*e.g.*, mRNA, genomic DNA) that encodes NOVX protein such that the presence of NOVX is detected in the biological sample. An agent for detecting NOVX mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to NOVX mRNA or genomic DNA. The nucleic acid probe can be, for example, a full-length NOVX nucleic acid, such as the nucleic acid of SEQ ID NOS:~~2, 9, 11, 19, 27, 35, 43, 51, 53, 61, 63, 65, 71, 73, 75, 83, 90, 92, 100 and 102~~ 1, 8, 10, 12, 18, 20, 26, 28, 34, 36, 42, 44, 50, 52, 54, 60, 62, 64, 70, 72, 74, 76, 82, 89, 91, 99 and 101, or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to NOVX mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein.